Barillas-Mury, Caroline 2020

Dr. Caroline Barillas-Mury Oral History 2020

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Dr. Carolina Barillas-Mury

Behind the Mask

November 3, 2020

Barr: Good morning. Today is November 3rd, 2020, and I have the pleasure of speaking to Dr. Carolina Barillas-Mury. Dr. Mury is the chair of the Mosquito Immunity and Vector Competence Section and the Director of the Malaria Research program at the National Institute of Allergy and Infectious Diseases (NIAID). Thank you very much for being with us today.

B-Mury: Thank you for the invitation. I'm very happy to be here.

Barr: During this time, you've been doing a lot of work on the BCG vaccine [Bacillus Calmette-Guerin vaccine] which was developed in the 1920s to protect against tuberculosis. So, what are some of the properties of this vaccine that you and others thought would be beneficial for those with COVID-19? It's really interesting.

B-Mury: The BCG vaccine contains attenuated mycobacterium bodies Mycobacterium bovis. It is a bacillum similar to the one that causes tuberculosis in humans but is attenuated so it doesn't cause disease. This vaccine has two effects: one, it protects particularly young people from severe tuberculosis, from systemic tuberculosis, so it's used in national campaigns all over the world. In most developing countries where tuberculosis has not been eradicated, all infants are given the BCG vaccine during the first months after birth.

Early on, this vaccine has two effects—one as I mentioned, the protection against tuberculosis—but what has become apparent in recent years is that it has a second effect, it also enhances the immune surveillance of the lung. There are several studies showing that BCG vaccination, particularly in the elderly, prevents pneumonias and it works also for pneumonias of viral origin. The BCG vaccine has been used for treatment of bladder cancer, because applying the BCG in the bladder activates the immune surveillance of the bladder, and when the cancer cells come, they are killed by the immune system.

It clearly has two effects, a specific one against mycobacterium bacteria, organisms similar to that you vaccinate with, and this gives cross-protection to mycobacterium tuberculosis. So, you use the mycobacterium which is mild and causes a very mild local skin infection but then this protects the lung from tuberculosis. That's one, but the second effect is broad as it's just enhancing immune surveillance and is nonspecific. It will help the lung deal better with most infections and appears to be very effective for viral infections.

The reason I have a background in this, is because I've been studying these kinds of broad innate immune responses and this enhanced immunity, or trained immunity, in mosquitoes, because this is a very old part of the immune system that insects also have. We have been working on this and I've been studying the mechanisms of how this works in mosquitoes. What has been found is that the same mechanisms are still there in humans. The question is how and why is this happening?

Barr: I was wondering how you became interested in this. Can you talk a little bit about your research, more into the study that you did with the BCG vaccine and COVID-19 mortality?

B- Mury: What happened was, I knew this literature about the broad protection or immune enhancement of immune surveillance in BCG. Then, as I was starting to look at the prevalence and the mortality of COVID-19, the reports in the New York Times showed all these maps of the different countries. It became apparent that the northern latitude countries, the wealthier countries, were having much more mortality from COVID-19 than lower income countries. That was unexpected because I would have thought that places where there's a lot of poverty and high population density will be more affected as the COVID-19 pandemic came into the country. However, in the Americas, the U.S. and Canada were the worst affected in terms of mortality, meaning, that many people were dying. This begged the question: Was there any epidemiological information on which countries are vaccinating infants with BCG, for how long they have been vaccinating, and how well these programs have been implemented in different countries?

We decided to do an association analysis, an epidemiological analysis, between the strength of the BCG vaccination program in a country and the mortality from COVID-19 early on in the pandemic. Because later on, different countries adopt different policies. This can greatly affect the number of cases and this will affect the mortality too. But early in the pandemic, before these governmental responses took effect, you can see what happened when the pandemic hit a country— how many died, how severe it was.

So we did that—I think we can go in more detail if you want—but the problem when you do this kind of analysis is that many different countries have many differences between them so it's hard to control for all of them at once. You have to consider population density, age of the population, wealth, access to medical care, time of arrival of the pandemic, and climatic conditions. You have all these confounding factors. The difficulty of doing this association is how you untangle or separate some of these variables to try to minimize these associated differences that can bias the results and give you a false correlation. This was the challenge of this kind of study.

Barr: So where did you get the data to do your project and can you speak more about how you went about your analysis?

B-Mury: I realized that to do this we had to do an epidemiological analysis. I got together with two other collaborators, with Alvaro Molina-Cruz who is also from NIH and he's done a lot of population genetic studies. We also got Luis Escobar and he's from Virginia Tech and he's an epidemiologist who has a lot of experience with dealing with large data sets. The three of us worked together.

I got involved in reviewing all the literature and background on this enhancement of immune surveillance and all this literature and the biology as to why this could be working. Together, also we decided which comparisons we were going to be doing. We tried to do very different comparisons, to see if all of them took us in the same direction or not. Then, we started also obtaining the data. Alvaro Molina-Cruz was instrumental in that he helped us a lot doing that part, because you have to go into all the different websites, as the information we used was based on public databases. So, you have to access, for instance, the Worldometer and see all the cases of deaths and then how they change over time for many countries. We had to go into the country databases to get data on BCG vaccination. We went to WHO historical data on BCG. Some countries are there but not all of them, so it was a lot of work assembling all of these and then having tables that were all with the same parameters and universal. Also, we had to do adjustments because instead of, for the broad analysis, when we first started doing broad analysis, you have to absolutely control for the time of arrival of the pandemic. If you compare deaths at a given date, it's not fair because the pandemic has not arrived in some areas, so it's very important to correct the mortality for the date of arrival. That means that you have to have the mortality data for many countries, for many days. In our case, we said we're going to use the number of deaths 25 or 30 days after the first death was reported in each given country. Since the date when this happened is completely different in each country, we compress data so that the timing of arrival of the pandemic will not bias the results. Also, for some of the analyses, first we analyze everyone together. Then to remove all these demographic variables, you can also put filters and say, “I'm only going to compare countries that have similar human developing indices, the age structure is similar, population density is controlled, etc.” And although we were really strict, and we found that that we still detected a difference, meaning even whether we did a course analysis or an analysis with filters to only compare socially similar countries, in both cases, we saw a very strong negative association between the strength of BCG vaccination and the mortality from COVID-19.

So, the BCG vaccine is not going to keep you from getting COVID-19, but it's going to reduce the chance that you die from it. That's what the data showed.

Barr: What did you use, any particular tools or programs in doing your analyses?

B-Mury: I did not do the statistical analysis myself, but basically it involved curating all the data and then doing a multivariate analysis with different packages. I really don't work with them because I did not do that part of the analysis. We found that, for example, if you knew nothing about COVID-19 and you had only demographic information about these countries, what we found is that, together, two parameters, the Human Development Index, which is a measure of well-being of a country, and the population density were the best predictors of COVID-19 mortality.

Population density makes sense, since the more people you have in a place, the more likely they are to bump into each other and get infected. That makes sense. But the wealth of a country was intriguing, because being wealthy was correlated with higher probability of dying from COVID-19. A potential explanation is that those countries that are wealthier have eradicated tuberculosis, so they stopped vaccinating with BCG.

If this BCG hypothesis is correct, then this could explain why, when you stop vaccinating with BCG, you also are removing the enhanced immune surveillance that you have in those countries which continued with the vaccination program. So, this could be a potential explanation of why this was happening.

I think it's not only BCG. We can talk about this at the end, but I think there are other variables. One has to consider, for example, the weather. I think there's increasing evidence that, as the winter sets in, there's very high prevalence of vitamin D deficiency in countries that have strong winters. That's true in the U.S. too. For example, it is much higher in minorities, as the darker your skin the more likely you are to have vitamin D deficiency. The prevalence [of vitamin D deficiency] is about 82% in African Americans, 60-something percent in Hispanics. And what they found in a study from Spain, is that about 86% of people that were hospitalized from COVID-19 have very low levels of vitamin D at the time of hospitalization in a study in Spain. They also found that if they gave them high doses of vitamin D, they could prevent the worsening of the disease. Basically, of those that got high doses of vitamin D, only 2% had to be moved to intensive care, while of the ones that did not receive the vitamin D, 50% ended up in intensive care.

So, I think the timing of when this pandemic hits you is very important. If it hits you right after winter when your vitamin D levels are at the bottom, and that increases your risk of severe COVID-19. This is very important. I think that everyone should check their vitamin D levels or at least take a basic supplement to make sure they don't have a deficiency. A thousand to two thousand international units a day is the recommended dose to make sure you don't have a deficiency. So, I think it's very important at this time that no one is vitamin D deficient, especially if the idea is that you need vitamin D to have your immune system in top form. When the vitamin D is low your immune system is not working well and cannot control this virus. I think that's very important.

Europe may have had the really bad combination of no BCG and low vitamin D, and those two things, together, caused this tremendous death rate. The same thing happened in New York City because you can see how many people died in New York, which is much higher than the mortality we've seen anywhere else. I think it was these two things. No BCG, so the innate immune system may have not been so active in adults, especially older individuals as the immune system gets weaker with age; children may be better protected. As you get older and weaker, the BCG apparently helps to reactivate this immunity. Then, if this pandemic hits you in February or March, when you have not had sun exposure all these months, particularly if you're African American with dark skin or you're Hispanic, these people have by far the highest mortality. If there is something we can do, so that if you get COVID-19, you will not end up in intensive care, but you stay at home. So that you may be sick for a while, but you get through it without major complications. That should be the goal.

Barr: Interesting. Is that what most surprised you about your findings or were there other things that you found very intriguing after doing your analyses?

B-Mury: We did very different comparisons because we thought, okay let's look at it from different perspectives, because there is no perfect way of doing this comparison. The first one we did was the course one. You take all the data from all over the world, although it's hard to control for all variables, but you put everyone together and with all the noise and all the variables, you see a strong signal. Then you add the filters and that reduces the number of countries you can consider because you're only taking countries that are socially similar. Although the number of countries is less, you still get a significant correlation. Then we said, "Let's look at what happened to the mortality in the first 25 days, not in the whole country, but because in the U.S. and in all Latin America most of the pandemic came in through airports from flights from Europe."

So, it (the arrival of the pandemic) happened in the states with the major airports—Georgia, New Orleans, and New York—and was very focal in the rest of the country. There was very little COVID-19 in the rest of the country compared to these three ports of entry. Then we compared these three states 25 days after the first deceased person was reported by the numbers with what happened in [the] state of Mexico state, including Mexico City. We also compared Rio de Janeiro and Sao Paulo states. We found that, although Latin America has much higher population density in these states, and these are poor states with favelas [low-income informal settlements] and very high housing density, the mortality from COVID-19 in these countries was much lower. This again does not fit what you would expect. I was afraid because I'm Latin American. I thought that if this pandemic would hit a poor country, it was going to be terrible, but initially, they had much less mortality. I'm talking about the first 25 days since the first death, so again this was unexpected.

So, no matter how you analyze it. Why [are] countries with more people that are interacting more with each other, due to higher density and with more poverty respond[ing] better to COVID-19? So again, these are poor countries that all have BCG vaccination because they still have tuberculosis to think about.

Then we say, "Now let's move to the new world as a whole because the pandemic arrived by airport at pretty much the same time, as these travelers from Europe arrived in the new world at the different airports." Then we normalize for the first 25 days after their first death, so that was highly significant.

Then we say, "Let's look at Germany." Germany was very interesting because Germany had been one country for 30 years but before that they had very different BCG vaccinations. They have a program which had a very short timeline, less than 20 years in West Germany, while in East Germany they vaccinated for a longer time and they only stopped when they unified. Before that they had been vaccinating for a long, long time, so that people that are 30 and older are very well vaccinated in East Germany but not in West Germany. When we compare the states of East Germany where BCG programs were active for a longer time there was significantly lower mortality than West Germany.

Then we took a look at a bigger scale. We said let's compare now all of Eastern Europe and Western Europe. We did that and again the mortality in Western Europe was nine times higher than in Eastern Europe. The latter countries were part of the Soviet Union and most of them maintained the tuberculosis vaccination program with BCG at birth because they still have some endemic tuberculosis, so they kept this program. Again, there was this big difference.

But Western Europe, and Europe in general, have a complex history because different countries vaccinated at different times. Some of them had a program, but they interrupted it at different times; some interrupted 10 years ago or 15 years ago or 30 years ago. How long they kept this campaign in each area was variable so we tried to combine all of this information into one number that would tell us how well this population was vaccinated. We call it the BCG index which takes into account the age and what percent of the population was vaccinated. At the extremes the evaluation goes from zero to one, so zero is, for instance, Italy or Belgium that never vaccinated anybody, so it's zero. Now, at the other extreme are some countries like Ukraine where they have vaccinated for 70-75 consecutive years, more than 98% of the population, so those are rated as one. Then we took all these numbers and we did a correlation analysis between BCG and mortality, we again saw a very strong correlation.

To be even more strict, we said, now let's just take socially similar countries in Europe and do this analysis, and then the correlation was very strong. The R square, which, if it was perfect would be one, (which is never perfect) but in this case was 0.88, which means it's extremely strong and the probability that this association is random is extremely low. This analysis says that every 10% improvement in the BCG index of the BCG program reduced COVID-19 mortality by 10%. So, there's even a quantitative effect of the level of the quality of the program with the level of death.

All of this together is telling you that there is a very strong association between BCG vaccination and reduced COVID-19 mortality. It doesn't show causality, just tells you that when one is high the other one is low. All epidemiological studies only tell you, as they say, there's a very important biological thing happening. It's like cigarette smoking. You show that those that smoke have higher cancer rates, but you haven't shown that smoke caused the cancer because maybe those that smoke do also something else that causes them cancer. The cause-effect is a difficult thing and for that you need clinical trials.

Barr: What are the implications of your findings? Do you feel you know it's most likely that the more developed countries, like the United States, are not going to start doing BCG-like vaccinations of its population?

B-Mury: Well, yes and no. What we discussed is, of course, the U.S. is not going to start vaccinating all the infants today with BCG. But would it be worthwhile vaccinating health workers with BCG? Would vaccinating adults with BCG give them at least one or two years of protection from severe COVID-19?

This is a big question and actually the Gates Foundation and several other institutions have funded a big clinical trial called "Activate" where they're doing this. They're going to immunize more than 10 000 health workers. They start in Australia and Netherlands, but they have run out of cases because the pandemic went away. They moved part of the study to Spain and Brazil. I think now they're continuing in the Netherlands because they have the second wave of cases. So, all the studies are on their way and they're following them and they are seeing if those that got the vaccine did better. The problem is that these studies take a while so these results will not be known until spring or late spring or early summer of next year. It is hard.

Also I've been involved in giving advice to a group of physicians in Guatemala City who are doing this for the health workers, not only doctors, but the ambulance workers, the drivers, the security, the secretaries that receive the patients because all of them are high risk of exposure. They are vaccinating a thousand health workers and then there are about 2,000 people who will not be vaccinated as they want to see if those who have received a vaccine are at a lower risk of complications. They're going to track them, so the study is underway.

These studies take a while, but I think it's very important. It begs [asks] the question, thinking about the future, if this gives broad protection from any virus. Maybe BCG vaccination is a good thing to do, especially for those 60 and older who have a weaker immune system. The thinking is that by having the BCG you will awaken or rejuvenate your innate immune system and your immune surveillance. It seems to work very well for the lungs so that then whatever a new pathogen comes along, even if you have never seen it, you will be able to deal with it. Children are good at it because all the pathogens they see are new because they're young, they're children. But for us, as you get older most of the bugs you've already seen. You've seen influenza, you've seen almost any infection you were going to have by the time your are 60.

As of the use of BCG as a way to rejuvenate the immune surveillance, particularly of the lung, there are several studies. There are small studies in Japan and Indonesia, and a new nice study as a collaboration between Greece and the Netherlands. The study in Europe shows that vaccinating people 65 and older reduces the risk of viral pneumonias by 80%. They took people that had been hospitalized for pneumonia and half of them received BCG and then they followed them for a year and those that received the BCG had 80% less viral infections that require hospitalization than the ones that did not. This study was finished and was published recently, but this was done before COVID-19. But everything indicates and the protections was from all viral infections so it suggests that this vaccination of the elderly could protect from severe COVID-19. You will still get COVID-19 but it will not put you in the hospital.

I would say there are three things that are really important: having good levels of vitamin D; maybe in the future BCG to see if that could work, but right now the studies are still underway; and wearing a mask. Wearing a mask is super important because, I think, even if it's not perfect, even a cloth mask helps. If you're wearing a mask, it does two things. If you have COVID-19, you're less likely to infect other people, so that's good, it's altruistic, but it also does something very important for you, that I think very few people talk about. It is that the dose of virus that you get infected with determines how sick you're going to get. So, if you're wearing a mask and someone coughs on you, and you still get COVID-19, but the dose you get is ten times lower, you're much less likely to end up in the hospital than if you inhale the full dose of virus. So, it's very important also because if you happen to get infected you will not get a severe disorder, you're much less likely to get severe disease. The other phenomenon that is happening is that there's been a lot of anectotal evidence, but this is there's no proof—that when you're wearing a mask and you inhale very low doses of COVID-19, maybe it is serving as a vaccine.

In Latin America, you have countries, for instance, like Guatemala (I'm from Guatemala) where they have a mandate to wear masks, so everyone is going around with their masks on. A lot of people are getting infected but there are very few people in the hospital. Imagine, as an example, that you need to inhale a thousand viruses to get infected, a minimum of one thousand to make you sick—I'm just making up a number. If you don't wear a mask and someone coughs on you maybe you will inhale 10,000 or 20,000 viruses so you get severely sick because your immune system has to deal with this huge dose of virus. But if you wear the mask, you will get a 1,000 or 1,500 and you did get sick but your immune system has much less to deal with. Now, if you get lucky and you're wearing your mask and you were far away from the person with COVID-19, and instead of inhaling a thousand you only inhale 100 or 200 viruses, it's not enough to make you sick, but if every day you take the metro and you inhale 200 viruses, after six months you may be vaccinated.

Barr: Interesting. I never thought of it like that. You may not be completely protected but you may be asymptomatic.

B-Mury: There have been outbreaks in factories, in meat processing plants, where they have everybody wearing a mask and they had a few people with symptoms. So, they did a screening and they found that more than half of the workers were infected and, because they were infected while wearing a mask, 95% of them were asymptomatic. So, almost everyone was infected didn't know it because they had no symptoms, because the exposure to the other colleagues at a low dose have been vaccinating most of them.

In my opinion the big tragedy in the States is to have politicized the use of masks. It is the simplest, the most useful tool that we have, and it protects others and it protects you. It may even give you a natural vaccine and protect you from severe COVID-19. Not wearing it is just not good, and it has nothing to do with politics; it has to do with caring about yourself, caring about your children also. I would say for this winter you need to get your flu shot, wear your mask, make sure you do not have vitamin D deficiency. I see very clearly that this is something we can do this winter while we wait for the vaccine. The vaccine will come but we'll have to get through this winter first, because we will not be getting this vaccine before the end of winter.

Barr: Definitely. Is there anything else that you feel is on the American people's radar in terms of COVID-19 that you can recognize from patterns from looking at COVID-19?

B-Mury: I think that this is a highly contagious virus and so, if we are out and about, the probability that eventually we will get infected is high. Your best protection is to be wearing a mask, so that if you get infected and you get very lucky, you will be getting a dose that is too low to infect you, and you will become resistant. If you are not so lucky and you do get it, you will get a milder disease. It's not about politics. We're in this together. Our enemy is the virus and we know what we can do not to allow the virus in our house. The first step to stay in, and if you need to go out, then put on your mask. Don't allow the virus in your house and don't allow viruses in your lungs. Wear a barrier which says, you're not entering my lungs. I'm gonna put this mask on, because, damn virus, you're not going to destroy my lungs, you're not going to destroy my life. We have to change our way of thinking. We are together in this fight against the virus that is the common enemy. When we fight together and when we come together, then we can handle this. We can greatly reduce the deaths this winter. Take your vitamin D if you need it, wear a mask, and make sure you don't get the flu together with COVID-19. Get your Flu vaccine.

I admire a lot of people. I admire, on a personal level, my mother, because the elderly have to isolate themselves. They've been through a lot more than we have; they have been through wars; they have been through a lot of things. So, what we are being asked to do is very little, just put a piece of cloth so that you protect lungs. It's not just everyone else who is your concern. It's your own lungs and the lungs of your children. It is hard but we're not being sent into a battlefield to give our lives. It is simple. The elderly are doing it and for them I think we have to do something. Even if you're young and you won't get sick, you may bring this disease to other people. You're part of the propagation. I think that's very important. I'm inspired by how disciplined and how resourceful at least my mother has been, always trying to find ways of keeping connected because I think we want to be physically distant but socially close, by phone and by zoom. For everyone's parents we owe it to them to do our best. We're doing it for ourselves for our children and for our parents.

Barr: Definitely. What are the next steps for you and others who are working on the BCG vaccination with COVID-19? In your article you said that you know more tests have to be done, and now it's kind of difficult that other factors have been introduced into the situation.

B-Mury: I think we've done what we can in terms of epidemiology. It tells you there's a very strong biological association here that is worth looking at carefully. The next step are the clinical trials which are already underway. There are several of them and there's going to be a lot of information coming up by next spring as to whether BCG really protects. This could be important before the next pandemic, maybe for the elderly getting a boost BCG vaccination every five years, will have you ready for whatever pandemic comes next. We don't know which one it is going to be.

You know, I work with malaria transmission and mosquito immunity and that's how I got into this. I'm not going to be intimately involved, but we're thinking of starting some collaborations. I know several groups at NIH are already using animal models of COVID-19. A model is critical so that you can understand how they are protected by BCG, what mechanisms lead to the pathways that offer protection, and how to stimulate these pathways in humans. When the next pandemic comes or if this pandemic keeps going longer—depends on how the vaccine goes— maybe vaccinating the elderly or the high-risk groups with BCG could be something that could buy time until we get this under control.

Barr: That's very interesting. Are you working on any other COVID-19 projects or initiatives right now?

B-Mury: No, I am not, because my area of expertise is innate immunity, mosquito innate immunity, and malaria transmission. We are investigating the molecular mechanisms in mosquitoes, since mosquitoes are simpler because they don't have antibodies. They don't have an acquired immune system, so we're working to understand the basic biology. Once we know how the system works, because this is the origin of the immune system, then this will give us tools to see if there are parallels between how innate immunity has evolved and how it's working now in humans. We develop new things, but we still have this ancestral form of innate immune surveillance. So, I think it's going to be very important to understand the basic principles which we can do better in mosquitoes. Once we know the basic principles of how this memory is established to enhance immune surveillance. Once there's been an exposure, the system remembers for a long time. If you think about the BCG, it seems like even 20 years after you're vaccinated with BCG, you're still better at fighting infections. If this hypothesis is correct, how do you remember this as it's not the normal immune memory, because this is a very primitive immune system? So, we're developing studies to understand where the memory is. which are the cells that remember? and how does this memory keep the new cells that appear more active and more ready to respond?

Understanding the basic biology of this system may have implications for human disease. We will collaborate with people that will do the mouse models with mouse COVID-19 because it is a better model. If we demonstrate that BCG does confer this protection in a mouse model, then we can understand how it's doing it, how it works.

Barr: This question is going to transition more into how you finally deal with COVID-19, rather than just professionally. What have been your personal challenges and opportunities during this very trying time?

B-Mury: I would say that the challenge for me has been that I love being in the lab and interacting with my team and with my colleagues on a daily basis. We have discussions; we have seminars. Science. I think of it like it's a tennis game where you bounce ideas back and forth, and as you do that, you are challenged with the comments, as other people give you feedback. This is how creativity and new projects come about.

When you are at home by yourself, you interact much less with people, so all these informal interactions are gone. Also, it's a lot of fun to sit down to have lunch with a colleague and have a nice discussion. It's a lot of fun and that's gone. So, I miss that.

I would say I try to keep in touch with my team. We have weekly meetings and sometimes I meet individually with other lab members one-on-one, but it's not the same. I think we've lost the interaction part. We have Friday seminars. But again, we are always a little bit detached. I think that has been challenging for me.

The other one is I was used to traveling. I'm from Guatemala, so all my family is abroad, and I cannot travel now. I cannot see them and that stresses me out. We don't know when I'm going to be able to do it. This is one of the challenges, and also the days get long because I have to do several things in my job. Some of it is administration, some of it is writing, and the other one is interacting with the students and postdocs. The other challenge is not working any more at the bench with them, or helping them troubleshoot. My day used to be very mixed and now the two most fun parts are gone, the brainstorming of ideas and the interaction with members of my team and working with them. Being with them at the microscope, looking at the samples and trying to figure out what we need to do is gone. What is left is the hard part which is writing—which is important, but it's a little hard and can be tedious, and I have to do the paperwork to run the lab. It is hard to remain motivated when the most fun parts of your job are on hold.

Barr: How have you been interacting with some of the fellows remotely? I'm sure that's a challenge. Have you developed tips that help solve the challenge?

Muri: Well, we do meet once a week. We have a lab meeting. Then when something comes up, we have smaller meetings, more informal with particular lab members. That's how we're handling it but it's not the same thing. For example, I have two new students that I've never seen in person. It's not the same; you hire someone who's been working for a couple of months in your lab and you've never seen them. We have tried to meet. When the weather was good in the Summer, we had an outside picnic and that went well, keeping socially distant so we all were wearing masks. We did a potluck, filled our plates and then we separated outdoors, so that we could eat and kind of talk at a distance. That was fun. We've done a couple of those but as Winter comes that's going to be harder because we can't be indoors all the time. Those are the challenges.

Also, I have a daughter that is a teenager at home and I think it's hard on young people, being very isolated at an age where they want to be with their peers more than anything else. It's hard to handle the changes in family scheduling and situation. On the other hand, on the positive side, I think that it gives you more flexibility because you can handle your schedule freely. You have to be careful to put an end to the day's work because people keep sending you things at any time because they know you're there. You cannot go anywhere. But I think that the flexibility and having more time to be closer with the family has been a good thing. You need to have things to break the routine because the days begin to merge, and all look the same. We've been trying to go at least in the car for rides and go somewhere to have a lunch or a picnic somewhere just to feel you we're outside, while the weather allows.

I think that being more flexible is also getting used to working from any place. For some things like writing, maybe being at home works better, in the sense that you're less interrupted, so you can focus better. Going forward, I may be telecommuting a couple of days a week and doing the part of my job at home that I do better at home and then going back to the lab to the things I enjoy with everyone else there.

Barr: You said that your mother is a source of inspiration for you during this time. Are there any others who you've looked to for inspiration personally and professionally?

B-Mury: One of my best friends from medical school. She's head of the infectious disease department at one of the biggest national hospitals in Guatemala. They have had to deal with COVID-19 with very little resources and trying to figure out how to treat these people without being sure what is going on. It's been very good because I have been able to refer them to resources from NIH or the new COVID-19 clinical information constantly coming up. For a scientist, our job is always to work in a territory where no one has ever been before. I think that I was able to play a good role finding and summarizing all this new information, so that I can discuss with the clinicians and then they can make better decisions in dealing with their patients. I really admire them because they had to develop the whole plan on how to treat the patients without infecting all the personnel. They are reference hospitals, so they receive all the people sick with other illnesses,and you cannot allow COVID-19 to come into the general hospital where people are already sick with something else. I admire them because they have worked very hard in reorganizing the health infrastructure in countries with very limited resources. I think they have been successful. They were able to use one of the big tools, namely, the use of masks, which has allowed them to give healthcare assistance to everybody without overwhelming the hospital system. This was a big breakthrough.

It's possible at some point to keep business open, but when cases are too much for a place, you can have curfews where businesses are open but by 9 pm you have to be home. I think it's a big risk going out at night. You go out with your friends; you're in a discotheque in a bar; you start drinking; you forget all the rules; and get everyone infected. Once you have two beers and you're dancing in a discotheque, you forget all the other recommendations. I think it is possible to open an economy but to limit some activities that are hot spots. I don't think we have to limit everything but at some point, when there are too many cases for the availability of beds in a hospital or too many people are dying, then you have to put some restrictions. But I think we understand better what the keys are. You don't have to close everything, but you may have to close particular hotspots. We learn a lot of how to do a more tailored response.

For a country as big as the U.S., you need to have a local policy adapted to the stage of the pandemic. I don't think that many people are aware that this was a tsunami that started on the East Coast with New York, New Orleans, and Atlanta, which were the seading points—the airports from where it spread to the East Coast, and then it caught fire in the Southern states, because there were a lot of young people out. So this started a fire with 10,000 independent fires. Now it is burning in the north. All these cases that are now in the Midwest, in the northern part, are going to start coming down to the Southwest. We still have one or two more ups and downs to go through.

I think that the measures that you needed in New York in February and March are completely different from what you needed in Montana at that time. You should not close businesses in Montana because there are cases in New York. It doesn't make sense. I think that coordination between states has been lacking, by not understanding how this wave of infections is moving. I think the graphics to show people where the cases are coming from are important. To let them know when the infections will come into their state. As the pandemic moves, we have to be aware where it is, and track it. The policies and what needs to be done should be very local because it changes over time. In other countries, like in Guatemala, they have installed what they call the COVID-19 stoplight. So, you have a green light that is really good, then you can get yellow, orange, and red. When you're in red, there are certain rules of what needs to be closed. Red means you're at the maximum peak, and you're about to overwhelm the system. You need to shut down some things. Once you go down to a certain level you can open certain things. Then you're going to orange. If orange goes well and then cases start going down, you move into yellow. They say, "Okay, you need to do this," and people are proud of where their county is. They say, "We brought it down; we were red, and now we're yellow." I mean it gives you a sense of where you are and what you have accomplished.

So, I do think that some system like that needs to be established in the States. I really think it's needed because part of the problem is, of course, if you live in Minnesota, you think everything is a hoax because what people are experiencing New York is not what you're experiencing. It's going to take six months to hit you, so for six months you're skeptical until it hits you. Then you realize it was not a hoax, right, but why should everything be closed for six months when the tsunami hasn't arrived? It doesn't make sense to close ahead of time, so I think that we need to have a dynamic and coordinated system with recommendations that are very clear for each stage of the pandemic, which is the same system in every county.

GB: I have two more questions. This question is a fun question. Have you tuned into any podcasts while during the pandemic?

CBM: Yeah. I, you know, I'm a nerd. I'm nerdy so I like "Quirks and Quarks." It's from the Canadian CBC, like the Canadian NPR let's say, and it's about topics in science, in general, and interesting things in science. I like "Science Friday"; sometimes I listen to "This American Life," but I mostly I like nerdy stuff. I'd rather hear about animals or the universe or something else. We're obsessed enough with what's happening to dwell on it all day because it can become an obsession. I mean [thinking about COVID-19] can become an obsession, and instead of helping, it just makes you more nervous, right, so I think you have to limit the amount of news you get every day or you start freaking out.

Also I like listening to music, and that's fine. Then, we have a group of friends —my best friends from medical school—with whom we get together on Sundays and we give each other support. We talk about what's happening with COVID-19, with our families, our work challenges, so that has been very good. It's four of us, and we've been really good friends for a long time. You know, I met them in '79 when we started college, and we have been friends ever since, so it was nice to reconnect. It's fun; you know it's like it's a virtual happy hour but also has a lot of elements in it. We also share data that we have on new COVID-19 treatments, or to discuss if something seems to be working or not. They're all medical doctors so it's fun. It's a fun group too.

GB: That's really nice. I hope that stays for you like this.

CBM: We'll see because I think that when we go back to normal, life will be busy again. I think there was something good about COVID-19, that things slowed down a little bit. Sometimes I felt that we were in this, you know like the hamster wheels, and it's just rotating fast. Then COVID-19 kind of stopped everything, so now it's like it's moving at a different pace, and I think that's important too, especially for science. I think sometimes you need to slow down and think carefully, and if you're stressed out and running all the time, you really are not in your most creative mode.

GB: Finally, is there anything else you would want to share as an NIH scientist and as a person dealing with the pandemic?

CBM: Yeah, I think that the first thing when we have a problem, the first stage is denial. It's not happening, right, but at this point, I don't think we can deny that this pandemic is here. So now, the next thing is, okay, we need to deal with it. So, I think that as a scientist, it is our job to defend the truth, even when sometimes truth is not fun. I mean, you know, we don't want to hear it. The first thing you need to do, is admit there is a problem, and then, second, begin to learn as much as you can about this problem to see what works. What has worked in other places [and] what mistakes have been done.

I think that having people with Vitamin D deficiency in a pandemic is a big mistake that can cost hundreds of thousands of lives and we cannot afford in the U.S to allow this to happen. It's very cheap, it's very inexpensive to take Vitamin D. Just make sure you're not deficient this winter especially if you're in an ethnic minority; the darker your skin, the more likely you are to be Vitamin D deficient because the sun doesn't process so well the Vitamin D. So, I think that communicating the basic facts, that's something that we need to. There's so much misinformation, people are overwhelmed. In my view, they often don't know what to do.

I've been thinking very hard [about] what do we need to do for this winter. You keep the normal things, right, like physically distancing when possible, wash your hands often, wear your mask. It may protect you, and if you get lucky, it may provide a natural vaccine or some resistance to the disease. You have to take your flu shot, to make sure you don't get COVID-19 and influenza at the same time, because that's not good. If we have to remember three things this winter: flu shot, mask, and do not allow your Vitamin D levels to go down. I think that if we do this, we can maximize our chances that we're all going to be here, sound and healthy, in good shape, and the vaccine will come, I think.

I don't know how fast. Also, if the vaccine is not looking so promising, we will have the results of the BCG trials. So maybe the BCG may may lower mortality. If we have to go through this pandemic, let's minimize the human cost. Eventually we will get herd immunity, but we cannot afford to have herd immunity without protection because it's too cruel, a devastating disease. Now if we can acquire it by wearing a mask and the vaccine, maybe [we'll acquire] herd immunity, but without the human cost—we get it [the infection], but we don't get sick; we don't get damaged, and we get protected. So, I think the two things that could give us that, are for sure, the Vitamin D and the mask. Depending on how the COVID-19 specific vaccines go, the BCG may become an option in the Spring. At least for those 60 and older, which are the groups with the highest mortality. It may be recommended for them, and we will know if that's a viable option. I think it's going to be very exciting. We're going to be talking about this pandemic for years, and we will learn a lot about immunity and how to deal better with the next one.

GB: Well, that's exciting. Thank you very much for .talking with me, and I wish you the best with your studies, and I wish that you and your family continue to stay healthy.

CB: Thank you too. Thanks a lot for the invitation.